



Comparative Study the Effect of Induction of General Anesthesia with Propofol Versus Thiopentone in Pediatric Age Group on Cardiovascular System

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Abstract:

Background:

We compared the hemodynamic responses of i.v. Propofol 2.5 mg/kg with thiopental 5.0 mg/kg in 41 healthy children during anesthesia induction in Imam Sadiq Teaching Hospital and Al Hilla General Teaching Hospital/ AL Hilla IRAQ from February 2014 to December 2016 .

Methods

Four groups were divided according to age and type of injectate received: group 1 (2 years), propofol (n = 9); Group II (2 years), thiopental (n = 9); group III (2–12 years), propofol (n = 12); and group IV (2–12 years), thiopental (n = 11). Anesthesia was maintained by spontaneous breathing with 70% nitrous oxide and 0.5% halothane in oxygen. Blood pressure and heart rate were monitored. Stroke volume was measured using pulse Doppler and echocardiography .

Results

Measurements were taken before induction and at 1-minute intervals for 5 minutes after induction. The reduction in mean arterial pressure was significantly greater after propofol (28–31%) than after thiopental (14–21%) (P = 0.001). There was no significant differences in reduction of cardiac index (10–15%) after induction between the two drugs (p=0.122).

The increases in heart rate and systemic vascular resistance due to activation of Baro receptor reflex were less after propofol than after thiopental alone. The baroreceptor reflex was more weakened in young 2-year-

olds than in older children. Induction of anesthesia with propofol is associated with a much greater reduction of arterial blood pressure compared to thiopental in both adults [1-4] and children [5-7]. It is one of the main criticisms of the use of propofol. In adults, the hypotension appears to be due to reduction of systemic vascular resistance [2, 4, 8, 9]. There is controversy about the direct effects on the cardiovascular system. However, this appears to have a slightly negative inotropic effect. Due to ethical and technical limitations, pediatric hemodynamic data is limited to noninvasive heart rate and blood pressure measurements [5-7], but these peripheral hemodynamic measurements are insufficient to describe the myocardium effects that result from the anesthetics [10]. With the development of echocardiography, this is now possible. The measures cardiac output non-invasively with high accuracy by combining echocardiography technology and the Doppler principle. Measurement of cardiac parameter using the Pulse Doppler technique. The echocardiography of proved to be of high quality correlation coefficient ($r = 0.90-0.98$) versus by dye dilution technique [11, 12]. In this study, this technique was used to compare the cardiovascular effects of intravenous anesthesia induction with Propofol versus thiopental.

Key words: Anesthetics: intravenous, propofol, thiopentone. Anaesthesia: paediatric. Heart: cardiac output. Measurement techniques: echocardiography.

PATIENTS AND METHODS

We examined 45 healthy children aged 8 months to 12 years (ASA I or II) expected for the proposed transaction. consent form were received from parents. Children with a History of allergies or side effects from premedication were excluded. The children whose hemodynamic variables are not obtained before induction or a venous cannula not inserted before induction were withdrawn from the study. All patients received premedication with oral diazepam syrup (0.4 mg/kg1). and EMLA cream (25 mg/g lidocaine) and on the backs of both hands, about 2 hours before anesthesia. The children were divided into groups two age groups: under 2 years and 2 years - 12 years. Children of all ages were assigned in double blind random mode to get one propofol 2.5mg kg1 or thiopental 5 mg kg-1 . Upon arrival in the anesthesia room, non-invasive An automatic measuring device was used and a 24 gauge needle were inserted into the vein in the opposite hand where the pulse oximetry probe is located was connected to continuous monitoring arterial oxygen saturation. The child was released constant and hemodynamic baseline measurements .The child was quiet or not. According to the basic records, the drug was injected for a period of time 20s. 1% lidocaine (0.05 ml) was added ,each 1 ml propofol immediately before administration. As soon as the child falls asleep – a face mask applied and anesthesia maintained at 70% nitrous oxide and 0.5% halothane in oxygen using a Jackson-Rees

Modified Ayre T piece. Hemodynamic variables were monitored at one minute intervals for 5 minutes after the end of the i.v. ETCO₂ concentration was monitored with a Capnometer Main stream attached to the face Mask. Fresh gas flow and ventilation have been adjusted in order to keep Concentration of end tidal CO₂ at a pressure of 4.7-6.0 kPa. blood pressure and heart rate were recorded. The stroke volume was determined by Ultrasound scanner with handheld Doppler Probe 5MHz. An inner diameter of the aorta aortic ring measured by two dimension echocardiography. Three measurements were taken and the aorta averaged Diameter. Pulsed Z-wave Doppler signals ascending aortas were identified and recorded by placing the transducer probe in the suprasternal area score. The converter was set to balance sent the sound beam as parallel as possible blood flow velocity vector. All calculations were done by the built-in program ultrasound. Doppler recordings e.g ECG recordings were recorded on videotape analyzed later. The blood flow velocity was calculated from Doppler equation:

$$V = \Delta f c / 2f_0$$

Any deviation of the transducer from the parallel axis of more than 20° angle was corrected by the formula:

$$V = \Delta f c / 2f_0 \cos \theta$$

where V = velocity of blood flow; Δ = change in

frequency; c = sound velocity in the blood; f₀ = transmitting frequency; θ = angle of insonance or the angle between the beam of ultrasound and the direction of blood flow. Stroke volume (SV) was computed by multiplying

Stroke volume was calculated by averaging measurements of three cardiac cycles.

Derived hemodynamic variables calculated from the variables measured included cardiac output, Stroke volume and cardiac index indicator. cardiac output was calculated as the product of the stroke volume and heart rate. The surface area was derived of the nomogram for infants and children [13]. Systemic vascular resistance (SVR) was calculated. with the following formula [14]:

$$SVR (\text{dyn s cm}^{-2}) = \frac{80}{\text{cardiac output}}$$

In order to compare the effects of two agents in two age groups of children, the patients were allocated to four groups:

group I: toddlers younger than 2 yr. who received propofol;

group II: toddlers younger than 2 yr. who received thiopentone;

group III: children aged 2-12 yr. who received propofol;

group IV: children aged 2—12 yr. who received thiopentone.

Data collected from patients of the same age group were compared using a two-tailed Student's t-test. THE number of restless children and side effects frequency were analyzed using the chi-square test. baseline hemodynamic variables were compared unidirectionally analysis of variance. Post-induction hemodynamic measurements were analyzed using replicates measure analysis of the variance for the difference between core values. The factor considered was the , anesthetics and age interaction and time After induction. Since there were no statistically significant interactions between age and agent used in anesthesia, data were collected from four groups the results was considered statistically significant in between groups simultaneously p value < 0. 05.

RESULTS

Four cases were excluded from the analysis because inappropriate Doppler recordings. From 41 children were examined, including 18 newborns (nine in group I, nine in group II) and 23 are older children (12 in group III and 11 of group IV). Patient Data and Report in each group, children who were restless from the sedation were identified Table 1.

It was not statistically significant differences in mean age, body weight and area range between groups I and II or between groups III and IV. There were more girls in groups III and IV. There were more anxious children ($P = 0.01$). groups I and II compared to groups III and IV (Table 1). The hemodynamic baseline variables did not differ significantly between groups I and II or between groups I and II Groups III and IV (Table 2). Average heart rate were larger ($P=0.001$) and vascular resistance values were higher ($P = 0.024$). The mean heart rate was stable in older children receiving propofol (Group III) or thiopental (Group IV). Over there was a significant difference ($P<0.001$). magnitudes of heart rate changes for two age groups groups . After the procedure, there was an increase in the stroke volume index Induction from to a maximum of 12% in young children after propofol (group I) and thiopental (Group II) .In older children, the stroke volume index decreased by a maximum of 13% in propofol group (group III) and by 15% in thiopental group (group IV). These changes did not differ statistically . The cardiac index of, which reflects the combined effects of heart rate and systemic vascular resistance, decreased significantly in all groups ($P = 0.005$) . In young children, the maximum decrease in cardiac index was 15% after propofol and 3% after for thiopental. In older children, the maximum reduction after each application was similar (10%).Systemic vascular resistance decreased significantly after induction in all four groups ($P = 0.001$) The maximum reduction was similar in the

TABLE 1 Patient characteristics (mean (range or SD)). Group I = less than 2yr, propofol; group II = less than 2yr, thiopentone; group III = 2—12yr, propofol; group IV = 2—12yr, thiopentone. BSA = Body surface area; Mood (a :c)= number of children agitated or calm. * $P < .05$

variables	Group I (n = 9)	Group II (n = 9)	Group III (n = 9)	Group IV (n = 9)
Age (yr)	1.2(0.7-2)	1.1 (0.7-2)	5.2 (2-12)	4.4(2-12)
Weight (kg)	10.6(1.3)	9.7(1.3)	18.8(8.5)	16.4 (6.4)
Sex(M:F)	9:0	7:2	10:2	6:5
BSA (m ²)	0.46 (0.04)	0.44 (0.06)	0.78 (0.24)	0.70 (0.20)
Mood (a:c)	7:2	5:4	4:8	1:10*

children who received propofol (15%) and those who received thiopental (16%). The decrease in systemic vascular resistance was almost three times greater in the propofol-treated older children (19%) than in the thiopental-treated children (7%). The differences between the four groups were not significant.

TABLE 2. Measured and derived hemodynamic variables before induction (mean (SEM)). Group I = less than 2yr, propofol; group II = less than 2yr, thiopentone; group III = 2-12yr, propofol; group IV = 2-12yr, thiopentone .SAP = Systolic, DAP = diastolic, MAP = mean arterial pressures; HR = heart rate; SVI = stroke volume index ; CI = cardiac index; SVR = systemic vascular resistance. ** $P < 0.01$; *** $P < 0.001$

variables	Group I N=9	Group II N=9	Group III N=12	Group IV N=11
SAP (mm Hg)	104.6 (5.3)	104.6 (5.3)	106.7 (5.0)	96.3 (3.9)
DAP (mm Hg)	71.6(3.6)	70.4 (4.6)	67.9 (3.0)	61.2 (3.3)
MAP (mm Hg)	85.7 (3.4)	85.3 (5.0)	85.3 (3.8)	75.5 (2.9)

SVR (dyn cm ⁵)	3129.7(332.9)	3413.7(289.6)	2290.6(186.1)	2203.6 (226.9)**
SVI (ml beat ⁻¹ m ⁻²)	33.5 (3.8)	34.1 (2.5)	41.7(1.6)	43.9 (3.8)
CI (liter min ⁻¹ m ⁻²)	5.2 (0.5)	4.9 (0.5)	4.2 (0.2)	4.6 (0.3)
HR(beat.min ⁻¹)	162.0(12.3)	143.7(10.1)	101.1 (5.7)	102.5 (4.2)***

DISCUSSION

We have shown that intravenous induction of anesthesia in children using propofol was associated with greater cardiovascular depression than an equivalent dose (see below) of thiopental. The degree of cardiovascular depression in young children was similar to older children. In this study, noninvasive pulsed Doppler and 2D echocardiograms were used to determine stroke volume and cardiac output. The measurements are highly reproducible [11, 15] and can accurately detect relative changes in cardiac output in individual patients.

It has been shown to correlate well with results from thermodilution and dye dilutions in infants and young children [12, 15, 16]. Determining cardiac output using M-mode echocardiography involves calculating the volume of the measurement in one dimension so that any errors made during the measurement can be amplified in subsequent calculations [17]. M-mode identifies the aortic root region only during valve movement, while two-dimensional echocardiography can identify both the aortic ring (orifice) and root region. At this point it is more compatible with the invasive techniques than with the aortic root measurements.

It has been suggested that pulsed Doppler is a better technique than continuous Doppler. Pulse Doppler measures velocity of flow by activating an interval at a specific location of the aortic opening, while CW Doppler measures velocity throughout the beam path and may encompass an area with a parabolic velocity profile, which can result in a misleading average space velocity of [12].

Equipotential doses are required to compare the cardiovascular responses between the two drugs.

We chose a thiopental dose of 5 mg kg⁻¹ as equivalent to propofol 2.5 mg kg⁻¹.

This ratio was based on previous work on their relative potencies of [18,19].

In this study, we found that the mean blood pressure reduction of propofol was significantly greater than that of thiopental in young children and in older children ($p=0.011$). This is similar to the finding in adults that propofol has a greater cardiovascular depressant effect than thiopental [2, 4]. Our blood pressure reduction scale with propofol was similar to that found in the previous studies [7,20,21]. In healthy adults, thiopental typically decreases blood pressure and cardiac output with or without a compensatory increase in total systemic vascular resistance [22-24] and a decrease in baroreceptor sensitivity associated with tachycardia [25]. Thiopental-induced cardiovascular depression is caused by a combination of vasomotor depression [26] and direct myocardial depression [27, 28]. Venous dilation leads to sequestration of blood volume on the venous side of the circuit and a reduction in left ventricular diastolic filling and stroke volume has also been suggested [29].

The children treated with thiopental in our study showed significant reductions in blood pressure and in cardiac index.

The heart rate changes were different in the two age groups. Mean heart rate increased in older children but decreased in younger children. When compared this study with other studies, thiopental in infants and children revealed a higher degree of myocardial depression [30], possibly due to a higher dose of thiopental (7.5-8.5 mg kg⁻¹) in the other studies. The mechanism of propofol-induced hypotension in adults have yielded conflicting results [31]. Lippmann et al. observed a

(35%) decrease in left ventricular work index and (18%) in cardiac work index using the thermodilution technique, without a significant decrease in systemic vascular resistance and pulmonary vascular resistance [4]. . Gauss et al. found, using echocardiography and end-systolic rate as an indicator of inotropy, that propofol induced hypotension due to simultaneous negative inotropy and afterload reduction [32]. Grounds et al. observed a significant reduction in total systemic vascular resistance by (18%) with minimal changes in heart rate and cardiac output using the thermodilution technique [2]. In this study, the magnitude of hypotension following the use of propofol was similar to that observed in adults [2]. This was associated with a significant reduction in cardiac index (10-15%) and systemic vascular resistance (15-19%). The heart rate of the older children did not change, while it decreased significantly in the newborns . More infants than older infants were crying upon arrival in the operating room, which may have led to an increase in sympathetic tone. We suspect that this impacted increased heart rate and systemic vascular resistance. Anesthesia weakens the sympathetic tone of which may have contributed to the greater heart rate reduction of in younger children. However, the heart rate was in the physiological range of. Baroreceptor reflexes were more impaired in young animals and humans anesthetized with halothane [33, 34] or nitrous oxide[35] than in adults. Therefore, it is possible that the difference in heart rate reduction around ,reflects greater baroreceptor impairment in younger children than in children over When comparing the two drugs, the heart rate reduction was greater with propofol than with thiopental. This suggests that propofol causes times more baroreceptor depression than thiopental consistent with previous studies in adult patients [36, 37]. It is believed that pediatric patients have limited ability to increase myocardial contractility and heart rate is an important factor in determining cardiac output [38]. However, the infants in this study experienced an increase rather than a decrease in stroke volume index, which was associated with a decrease in heart rate. This suggests that the myocardium can increase stroke volume in this age group. Ventricular diastolic filling time and stroke volume are inversely related to changes in heart rate mediated by baroreceptor reflexes. The net effect of these hemodynamic responses was to produce a non-significant difference in the reduction in cardiac index in the four groups. As with thiopental, no compensatory increase in systemic vascular resistance was observed with propofol

Premedication with midazolam was necessary to reduce anxiety and to enable baseline hemodynamic measurements. We used a dose of 0.2 mg kg⁻¹. [39].Pre-medication use is not associated with significant cardiovascular depression [40]. Any incidental hemodynamic effects due to premedication should be considered relevant when these inducers are used in a clinical setting

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